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Inguinal Lymph Node Metastases From Rectal Adenocarcinoma

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Background and Objectives: The prognosis of patients with inguinal lymph node metastases from rectal adenocarcinoma is poor. The purpose of this study is to analyze the clinical behavior and response to different therapies in a group of these patients.

Materials and Methods: The medical records of 32 patients with inguinal lymph node metastases from rectal adenocarcinoma, diagnosed between January 1985 and December 1996, were retrospectively analyzed. The cohort was divided into: Group A (synchronous), and Group B (metachronous), according to the time of diagnosis.

Results: There were 17 males and 15 females, with a mean age of 53.5 ± 13.8 years. Bilateral inguinal lymph node metastases were diagnosed in 17 patients, and unilateral in 15 patients. Fourteen of 18 patients in Group A (78%) and 13 of 14 patients (93%) in group B, respectively, had concomitantly extrapelvic metastatic disease. Seventeen patients in Group A treated with colostomy + chemoradiotherapy (45 Gy/20 fractions to the pelvis and groin area + 5-fluorouracil 450 mg/m^2/weekly) had a progressive metastatic disease; the remaining patient was lost to follow-up after an abdominoperineal resection plus superficial groin dissection. Median survival was 8 months (range, 4–30 months). Overall 5-year survival was 0%. Ten patients in Group B were treated with chemoradiotherapy (50 Gy/25 fractions + 5-fluorouracil 450 mg/m^2 + leucovorin 30 mg/m^2); three patients received supportive care only, and one patient was treated with a groin dissection. All of them died of disseminated metastatic disease at a median of 13 months (range, 6–57 months). Overall 5-year survival was 0%.

Conclusion: The presence of inguinal metastases in patients with rectal cancer heralds systemic disease and, due to a poor response to the different therapies, only palliative treatment should be indicated.

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KEY WORDS: **rectal neoplasm; radiation therapy; chemotherapy; surgery; metastases**

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INTRODUCTION

Inguinal lymph node metastases from rectal adenocarcinoma are uncommon. When they occur, they are generally accompanied with hepatic/pulmonary metastases and/or pelvic recurrences, because of a dual cross-drainage system to the mesenteric and para-aortic lymph nodes through the perirectal and pararectal lymphatic vessels, and to the inguinal lymph nodes through the perirectal, perianal, and pudendal lymphatic vessels [1,2]. Lymphatic dissemination from tumors located in the lower third of the rectum are complex and unpredictable.

Current literature does not contain much information on the choice of therapy; since average survival in these patients is 13.5 months, the recommended treatment is merely palliative [3,4].

The purpose of this study is to analyze the clinical biological behavior and response to therapeutical interventions in a group of patients with inguinal metastases from primary rectal adenocarcinoma.

MATERIALS AND METHODS

A retrospective analysis was performed on 32 patients with inguinal lymph node metastasis from rectal adenocarcinoma, treated from January 1985 through December 1996 at a single institution.

Clinicopathological variables analyzed included: primary tumor site; histological type; degree of differentiation; recurrence patterns of the primary tumor (pelvic, distant, or combined) at the time of diagnosis of the inguinal metastases; primary tumor treatment and therapeutic interventions to groin metastases; response to therapy; and status of the patients at the time of death or study closing date.

Synchronous metastases were defined as those concomitantly present with the primary tumor or during the first 12 months of follow-up. Metachronous metastases were defined as those that occurred 12 months after primary tumor treatment. Survival was calculated with the Kaplan-Meier method and differences between groups were established by the log-rank test.

RESULTS

There were 17 men and 15 women with a mean age of 53.5 ± 13.8 years (range, 28–72 years). Primary tumor was located in the lower third of the rectum (0–5 cm from the anal verge) in 24 patients and, in the remaining patients, tumors were located 6 cm or higher above the anal verge. The histological varieties are shown in Table I. Distribution according to the degree of differentiation of the primary tumor is shown in Table II. Inguinal lymph node metastases were located in: *right groin,* 8 (25%); *left groin,* 7 (22%), and in *both groins,* 17 (53%).

Patients were divided into two groups: (1) synchronous metastases (n = 18), and (2) metachronous metastases (n = 14). Twenty-four patients (75%) had histological confirmation of inguinal metastases through an excisional and/or incisional biopsy. Diagnosis of the remaining eight patients (25%) was clinical, and was not corroborated, due to the fact that metastases diagnosis already existed in another anatomical site; these patients all had pelvic-perineal recurrences; liver metastases (n = 4); spine metastases (n = 2); ovarium (n = 1), and axilla (n = 1). Twenty-seven patients (84%) had pelvic recurrences or extrapelvic metastases, together with inguinal metastases.

TABLE I. Histological Type of Primary Tumor

Type	Number
Adenocarcinoma	22
Mucinous	4
Signet ring cells	3
Adenosquamous	1
Undifferentiated	1
Clear cells	1
Total	32

TABLE II. Degree of Differentiation

Degree	Number (%)
Moderately	17 (53)
Poorly	8 (25)
Well	6 (19)
Undifferentiated	1 (3)
Total	32 (100)

Group A

Fourteen of 18 (78%) patients had inguinal metastases concomitantly with distant extrapelvic metastases, as shown in Table III. Fourteen of these patients were treated with transverse colostomy plus radiation therapy (45Gy in 20 fractions + 5-fluorouracil (5-FU) 450 mg/m^2/weekly); in this group of patients, median survival was 8 months (range, 3–16 months); all of them developed a progressive metastatic disease; and all died with disseminated tumor activity. Inguinal metastases, as the only site of metastases, were detected in four patients: three of them had a rectal tumor fixed to the pelvis and were treated with 45 Gy radiotherapy in 20 fractions; two of them concomitantly received 5-FU at doses of 450 mg/m^2/on days 1–5, and 28–32 of radiotherapy. Diverting colostomy was performed on all patients; they had a progressive disease in the groin and pelvis and died of tumor activity 4, 16, and 30 months of follow-up. In the remaining patient, the rectal tumor was clinically resectable; therefore, an abdominoperineal resection plus groin dissection was performed. His surgical specimen had a mucinous adenocarcinoma metastatic to seven lymph nodes; the groin dissection specimen had two metastatic

TABLE III. Sites of Distant Metastatic Disease in Patients With Synchronous Inguinal Metastases From Rectal Adenocarcinoma (Group A, n = 18)

Location	Number of patients
Spine	3
Liver	3
Liver + lung	3
Retroperitoneum	2
Ovary	1
Spine + retroperitoneum	1
Axilla + thigh + spine	1
Total	14

lymph nodes. This patient received 50 Gy of postoperative radiotherapy delivered to the pelvis plus groin area in 25 fractions. The patient was lost to follow-up 4 months later with no evidence of tumor activity in the pelvis or in the groin. The overall median survival was 8 months (range, 4–30 months); overall 5-year survival was 0% (Fig. 1).

Group B

All 14 patients were treated with curative radical surgery to the primary tumor. Abdominoperineal resection was performed on 12 patients and pelvic exenteration on two. The primary tumor was staged as follows: T3, N2, M0 (n = 7); T3, N0, M0 (n = 5); and T4, N0, M0 (n = 2). Three of 14 patients received postoperative radiotherapy at a dose of 50 Gy in 25 fractions delivered to the pelvis, two received adjuvant chemotherapy with 5-FU at doses of 750 mg/m^2 weekly for 6 months, and one received preoperative radiotherapy and chemotherapy (45 Gy in 20 fractions + 5-FU 450 mg/m^2 on days 1–5 and 28–32 of radiation therapy). All developed inguinal lymph node metastases at a median of 26 months (range, 12–53 months) from the primary tumor treatment. At the time of ILNM diagnosis, 13 patients (93%) presented with metastatic disease. The sites are shown in Table IV. Treatment of the inguinal metastases was as follows: radiation therapy 50 Gy in 25 fractions to the pelvis and groin area plus 5-Fu 450 mg/m^2 plus leucovorin 30 mg/m^2 (n = 10) and only supportive care (n = 3). The median survival of these 13 patients was 13 months (range, 6–44 months). The remaining patient had isolated inguinal metastases at 26 months of follow-up, and was treated with a superficial groin dissection, but 44 months after follow-up he developed liver metastasis and died of the disease 57 months after groin dissection. The overall median survival after the diagnosis of ILNM was 13 months (range, 6–57 months). Overall 5-year survival was 0%, and no difference was found between the groups (Fig. 1).

DISCUSSION

Inguinal lymph node metastases from rectal adenocarcinoma generally herald an extrapelvic metastatic disease, as has occurred in the current series, where 84.5% of the patients had metastatic disease concomitantly with inguinal metastases. Groin metastases arise from locally advanced primary or recurrent rectal tumors with proximal lymphatic obstruction and retrograde dissemination to inguinal lymph nodes through the external iliac and femoral lymphatic vessels [5]. They can also occur via primary drainage of tumors infiltrating the anal canal, as shown in cases such as those with isolated inguinal metastases from epidermoid carcinoma of the anal canal [6,7].

However, the latter pattern of dissemination is rare, and is only explained in isolated reported cases of long-term survivors after groin dissection for metastatic rectal adenocarcinoma. Graham and Hohn [3] reported a survivor free of disease at 50 months [3]. Avill reported an 8-year survivor after abdominoperineal resection and bilateral inguinal dissection [8]. In our series, one patient developed isolated metachronous inguinal metastases and was treated with superficial groin dissection. This patient was the only long-term survivor, but after 44 months of follow-up he developed liver metastasis and died of hepatic failure.

Most inguinal lymph node metastases arise from low rectal tumors, the majority of which are bulky and infiltrate the anal canal. These tumors can be confused with anal adenocarcinoma in any of the three variants: rectal, anorectal fistula, and anal glandular type, which also has predilection for inguinal lymph node metastasis [9]. Similar to primary rectal adenocarcinoma, groin metastases from anal adenocarcinoma herald a disseminated disease with a 5-year survival of less than 20% [10,11].

In the current series, there were no statistically significant differences in the median survival of patients with synchronous and metachronous inguinal metastases (8 and 13 months, respectively). This median survival is similar to the 10.5 months and 7.5 months reported by Mesko et al. and Graham and Hohn [3,4], respectively.

Even though 75% to 85% of these patients have disseminated metastatic disease at the time of diagnosis of inguinal metastases, there is a small but definitive group of patients with isolated groin metastasis who may achieve long-term survival with a groin dissection. Further studies are needed to identify this group of select patients. Ultrasound, CT scan, and Nuclear Magnetic Resonance are not capable of detecting metastases of less than 1 cm in size. Recently, immunoscintigraphy or radioimmunoguided surgery have shown an improvement in the detection of micrometastatic deposits [12,13]. Also, the use of molecular biologic determinants such as p53 or K-ras specific mutations in codon 12 and 13 in the tumor tissue could potentially be used as a tool to appropriately identify this selected group of patients amenable for an aggressive approach [14,15].

As has been previously reported, the results of the

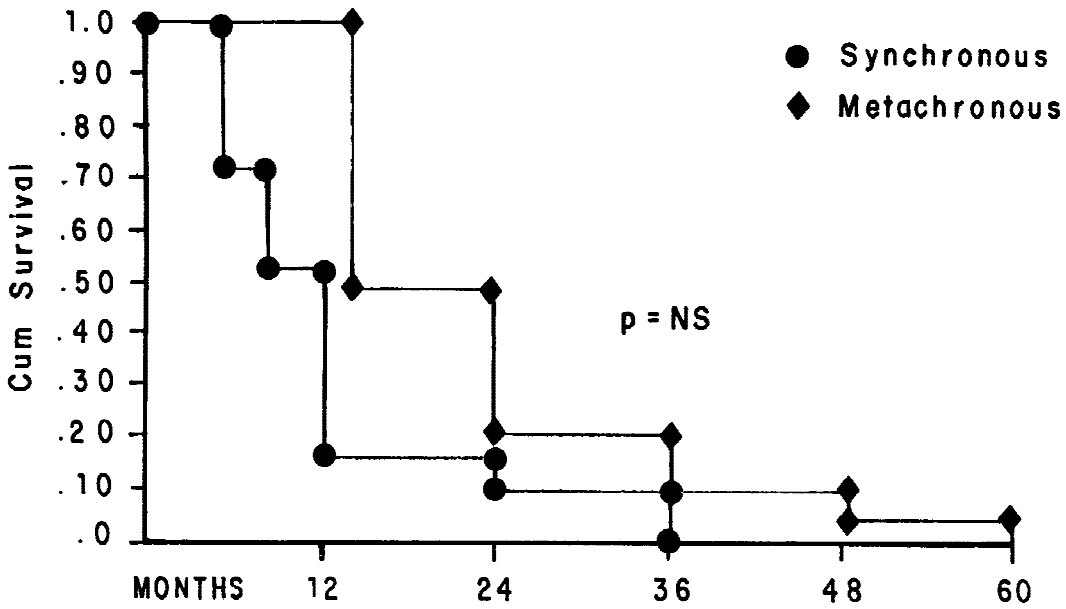

Fig. 1. Five-year survival in each group according to the Kaplan-Meier method, no difference between two groups ($P = 0.36$) (synchronous, 18; metachronous, 14). NS, non significant.

TABLE IV. Sites of Distant Metastatic Disease in Patients With Metachronous Inguinal Metastases From Rectal Adenocarcinoma (Group B, n = 14)

Location	Number of patients
Pelvis + peritoneum	3
Liver	3
Spine	2
Lung	2
Gingiva	1
Pelvis + stoma + peritoneum	1
Tongue + liver	1
Total	13

current series confirm that patients with synchronous or metachronous inguinal metastases from a rectal adenocarcinoma have a poor prognosis. The response to chemotherapy or radiation therapy, alone or combined, is unsuccessful, and therefore, the treatment of inguinal lymph node metastases from rectal adenocarcinoma, whether synchronous or metachronous, should be considered as palliative.

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